

KO 1 RBB-013 p 53 knock out mice Received - placed on water bottles.

Homozygous - DOB [5 males, 1 female] B6, 129 Tr p53 t mity B6N3F6 genetics Male # 412/413-8 p53/p53

Heterozygous - DOB [5 males, 1 female] (C57b1/6J male \times 129/sv+<p>+<c>+<Mfg-S1J> female) Female F2

- placed on Tempol or sugar water
Tempol - 58 mM [bottles hold 200 ml -4 gms + 400 ml water + 4 tsp sugar]
Control = 200 ml water + 1 tsp sugar

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LEYDIG, VOIT & MAYER, LTD EXHIBIT 1

kO 1 RBB-013
p 53 knock out mice
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Humozygous - DDB [5 maiss, 1 female] 86, 129 Tr p53 t mity 86N3F6 genetics Male # 412/413-8 p53/p53

Heterozygous - DOB [5 males, 1 female] (C5751/6J male x 129/sv+kp>+kc>+kl/fg-31J/ female) Female F2

- placed on Tempol or sugar water
Tempol - 58 mM [bottles hold 200 mi -4 gms + 400 mi water ÷ 4 tsp sugar]
Control = 200 ml water ÷ 1 tsp sugar

Age/Weight controls C5751/6J 5 males; 5 females 10/92852 D08 - Jackson Lab mice 129/5y-*Trp53tm17yi* [JR2080]

Developed in the Laboratory of Dr Tyler Jacks at the Center for Cancer Research, Massachusetts Inst of Technology.

129-derived D3 ES cell line. Founder mouse crossed to 129/Sv.

Stran is maintained by mating heterozygous siblings.

Homozygous mice develop tumors (mainly lymphomas) at 3–6 mo of age. Heterozygous mice develop tumors about 10 mo of age.

Mouse	Cago	Type	Sex	Tx	DOB	Tx Date	TIME Drug	Sac Date	TIME Death
01	01	-/-	M	C			21	8/5/96	109
02	01	-/-	M	C			21	8/5/96	109 / -
03	02	-/-	F	C	,	•	84	10/7/96	172 / -
Q4	03	-/-	M	T		Ē	21	8/5/96	109
0,5	03	-/-	M	T			112	11/4/96	200 ✓
06	03	-/	M	T	•		127	11/19/96	215 -
1 3	07	-/-	P	C			38	8/22/96	97 🗸 🗕
14	07	-/-	F	C			35	9/30/96	136 /-
17	09	-/- ·	F	T			92	11/26/96	175 /-
18	09	-/-	F	T	. ,		177	2/19/97	260 🗸
21	11	-/-	F	C			14	12/9/96	81 /-
22	12	-/-	F	T			121	3/26/97	176 -
27	15	-/-	F	E		5.17 th	35	1/27/97	105 -
25	14	-/-	F	T			133	5/5/97	182 -
29	17	-/-	F	T			41	4/13/97	97 v -
38	22	-/-	F	T	₹		34	4/13/97	97 -
31	19	-/-	F	C			126	7/14/97 .	182 -
33	20	- /	M	C			37	4/16/97	93/-
34	20	-/-	M	E			126	7/14/97	182
37	21	-/-	M	T			70	5/19/97	126/ —
39	23	-/-	M	T		3 0	109	6/27/97	161 /-

KO I AUTOPSY NOTES

Box 1 - Control:

mouse 1 - ascites and a large fluid-filled abdominal mass. mouse 2 - small neck tumor

Box 3 - Treated:

mouse 1 - 4 tumors; 2 neck and 2 under forelegs.

Box 7 - Control:

mouse 1 - extremely large neck tumor.

Box 7 - Control:

mouse 2 - neck tumor.

Box 2 - Control:

mouse 1 - tumor under Rifereleg.

Box 3 - Treated:

mouse 2 - large mass enveloping at upper lobes of lungs.

Box 3 - Treated:

mouse 3 - small tumor under chin; extremely large sipeen. L. kindey misshapened because of the spleen.

Box 6 - Treated (+/+):

mouse I - control tissue.

Box 9 - Treated:

mouse ! - enlarged spieen; small petechial hemorrhages along all lung edges; hemorrhagic cyst on L ovary; mass of milky material along abdominal midline.

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KO I AUTOPSY NOTES

Box 11 - Treated:

mouse 1 - severe weight loss; no visible tumors.

Box 15 - Control:

mouse 1 - tumors in thoracic cavity.

Box 9 - Treated:

mouse 2 - tumor in L groin; enlarged spieen; 3 1cm lymph nodes in abdomen.

Box 12 - Treated

mouse i - tumor above L eye; enlarged spleen.

Box 17 - treated

mouse 1 - enlarged sipeen, tumor in thoracic cavity.

Box 22 - treated

is mouse 1 - tumor in thoracic cavity.

Box 20 - control

mouse 1 - tumor in thoracic cavity.

80x 14 - treated

mouse !- tumor in thoracic cavity.

5/19/97:-

Box 21 - Treated

mouse 1 - soft tumor [2 cm] on back over L hip

6/26/97 -

Box 23 - Treated

mouse 1 - tumor in thorax, enlarged spleen.

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KO 1 AUTOPSY NOTES

7/14/97 Box 19 - Control
mouse 1 - enlarged spieen

Box 20 - Control mouse 2 - ear lesion on L, appeared to be a small tumor; enlarged spleen.

Pathology/Histotechnology Laboratory Pathology Report

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INVESTIGATOR: Deluca/Mitchell

MISTO #:

97-118120

- Malignant lymphoma, lymphoblastic. Tissue submitted is likely thymus. 3-1
- 3-2 Two slides submitted. Spleen. Two neoplasms: hemangioscoma and lymphoblastic lymphoma which involves primarily the white pulp. Also present are increased extramedullary hematopoiesis, moderate and angiectasis, moderate, multifocal. Mandibular I.n. - Lymphoplastic lymphoma. Salivary gland - Lymphoblastic lymphoma.
- Lung Hemangiosarcoma, metastatic; hemorrhage, moderate, multifocal. The septa have 9-1 numerous lymphocytes; this could represent a leukemic infiltrate but other lymphoid organs from this mouse should be evaluated before this diagnosis can be definite.
- 9-2 Spleen - Lymphoblastic lymphoma. Lymph nodes, inguinal and abdominal -Lymphoblastic lymphoma.
- 15-1 Thymus - Lymphoblastic lymphoma,

Miliam K. anver

Comments: Lymphoblastic lymphoma is the most common hematopoietic neoplasm in p53 KO mice.

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PERCENT SURVIVAL

